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To: EBENEZER SACKEY
Location: REM-5B31 / Mailbox 5C18
Art Unit: 1624
Thursday, January 10, 2008
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Case Serial Number: 10 / 532331

From: JAN DELAVAL
Location: EIC1700
REM-4B28 / REM-4A30
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jan.delaval@uspto.gov

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SEARCH REQUEST FORM

Requester's Full Name: Ben Sackey Examiner #: 73489 Date: 1/9/08

Art Unit: 1624 Phone Number: 2-0704 Serial Number: 10/532,331

Location (Bldg/Room#): Nan 5B31 (Mailbox #): 5C18 Results Format Preferred (circle): PAPER DISK

****

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

Title of Invention: 1-(4-Benzyl-piperazin-1-yl)-3-phenyl-propenone deriv.

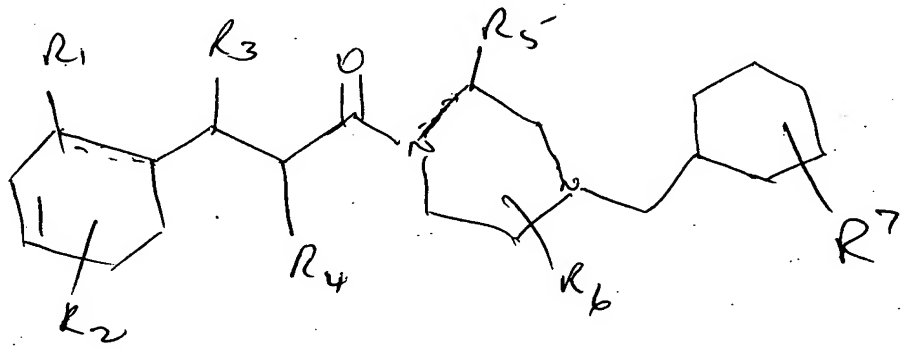
Inventors (please provide full names): Bollbuck et

Earliest Priority Date: _____

Search Topic:

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known.

For Sequence Searches Only ***Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.***



Please note claims 2 and 3.

Thanks.

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Searcher Location: _____

Date Searcher Picked Up: 1/10/08

Date Completed: 1/10/08

Searcher Prep & Review Time: 20

Online Time: +25

Type of Search

_____ NA Sequence (#)

_____ AA Sequence (#)

✓ Structure (#)

_____ Bibliographic

_____ Litigation

_____ Fulltext

_____ Other

Vendors and cost where applicable

✓ STN _____ Dialog

_____ Questel/Orbit _____ Lexis/Nexis

_____ Westlaw _____ WWW/Internet

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___ Commercial ___ Oligomer ___ Score/Length

___ Interference ___ SPDI ___ Encode/Transl

_____ Other (specify)

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FILE 'REGISTRY' ENTERED AT 14:23:39 ON 10 JAN 2008
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STRUCTURE FILE UPDATES:    8 JAN 2008  HIGHEST RN 960198-43-0
DICTIONARY FILE UPDATES:   8 JAN 2008  HIGHEST RN 960198-43-0

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L19             STR
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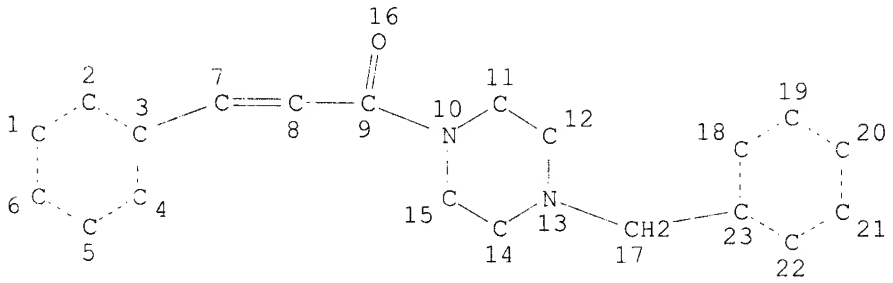


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CONNECT IS E2  RC AT   8
CONNECT IS E2  RC AT  12
CONNECT IS E2  RC AT  15
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC  13
NUMBER OF NODES IS  23

STEREO ATTRIBUTES: NONE
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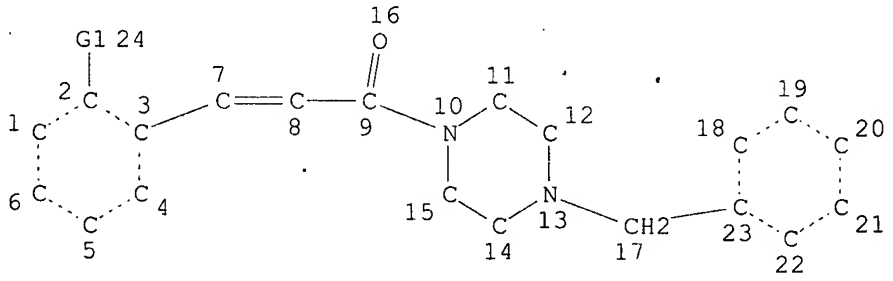

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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

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RSPEC 13
NUMBER OF NODES IS 24

STEREO ATTRIBUTES: NONE
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SEARCH TIME: 00.00.01

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		E	EDER/AU
L3	2	S	E3
		E	EDER J/AU
L4	207	S	E3-E7,E15,E19
		E	HENG/AU
		E	HENG R/AU
L5	21	S	E3,E4
		E	REVESZ/AU
		E	REVESZ L/AU
L6	157	S	E3-E5
		E	SCHLAPBACH/AU
L7	23	S	E4,E5
		E	WALCHLI/AU
L8	2	S	E20
		E	NOVARTIS/CO
		E	E5+ALL
L9	74857	S	E2+RT OR E2-E211/PA,CS
		E	NOVART/CO
L10	6623	S	E4-E6/PA,CS,CO
		E	NOVAR/CO
L11	1	S	E11/PA,CS,CO

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L17               STR L15
L18            42 S L17
L19               STR L17
L20            20 S L19
L21           398 S L19 FUL
                  SAV TEMP L21 SACKEY532A/A
L22           141 S L14 AND L21
L23               STR L19
L24               STR L23
L25             7 S L24 SAM SUB=L21
L26           148 S L24 FUL SUB=L21
                  SAV TEMP L26 SACKEY532B/A
L27           134 S L26 AND L22
L28             7 S L22 NOT L27
L29             1 S NCNC2-C5/ES AND L21
L30             1 S NCNC2-C6/ES AND L21
L31            17 S NCNC2/ES AND L21
L32            10 S L31 NOT L27-L30
L33           151 S L27-L32
L34            14 S L26 NOT L33
L35           165 S L26,L33,L34
L36            17 S L35 NOT L26
L37             7 S L36 AND L14
L38           165 S L35,L37

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                  E WAELCHLI/AU
L41            31 S E26,E27,E29,E30
L42             3 S L39 AND L41
L43             3 S L40,L42
L44             0 S L39 AND PY<=2002 NOT P/DT
L45             1 S L39 AND (PD<=20021025 OR PRD<=20021025 OR AD<=20021025) AND P
L46             1 S L45 AND L39-L45
L47             2 S L43 NOT L46

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L48             3 S L38
L49             1 S L48 AND (PD<=20021025 OR PRD<=20021025 OR AD<=20021025)
L50             2 S L48 NOT L49

     FILE 'REGISTRY' ENTERED AT 14:23:39 ON 10 JAN 2008

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CA INDEXING COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 10 Jan 2008 (20080110/PD)
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FILE LAST UPDATED: 10 Jan 2008 (20080110/ED)
HIGHEST GRANTED PATENT NUMBER: US7318238
HIGHEST APPLICATION PUBLICATION NUMBER: US2008010713
CA INDEXING IS CURRENT THROUGH 10 Jan 2008 (20080110/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 10 Jan 2008 (20080110/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Oct 2007
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Oct 2007

=> d l49 bib abs hitrn fhitstr

L49 ANSWER 1 OF 1 USPATFULL on STN
AN 2006:203118 USPATFULL
TI 1-(4-Benzyl-piperazin-1-yl)-3-phenyl-propenone derivatives
IN Bollbuck, Birgit, Weil am Rhein, GERMANY, FEDERAL REPUBLIC OF
Eder, Jorg, Rheinfelden, GERMANY, FEDERAL REPUBLIC OF
Heng, Richard, Hegenheim, FRANCE
Revesz, Laszlo, Therwil, SWITZERLAND
Schlapbach, Achim, Lorrach, GERMANY, FEDERAL REPUBLIC OF
Walchli, Rudolf, Basel, SWITZERLAND
PI US 2006173004 A1 20060803
AI US 2003-532331 A1 20031024 (10)
WO 2003-EP11848 20031024
20050422 PCT 371 date
PRAI GB 2002-24917 20021025 <--
DT Utility
FS APPLICATION
LREP NOVARTIS, CORPORATE INTELLECTUAL PROPERTY, ONE HEALTH PLAZA 104/3, EAST HANOVER, NJ, 07936-1080, US
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 4060
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A compound of formula (I), or a pharmaceutically acceptable salt or ester thereof, wherein the symbols have meaning as defined, which are antagonists of CCR-1 and which find use pharmaceutically for treatment of diseases and conditions in which CCR-1 is implicated, e.g. inflammatory diseases. ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **685534-33-2P 685534-35-4P 685534-56-9P**
685535-44-8P 685535-79-9P 685535-81-3P
685536-74-7P
(CCR-1 antagonist; preparation of (benzylpiperazinyl)phenylpropenones as CCR-1 antagonists for treatment of inflammatory and autoimmune diseases)
IT **685534-20-7P 685534-25-2P 685534-26-3P**
685534-28-5P 685534-29-6P 685534-30-9P
685534-31-0P 685534-32-1P 685534-34-3P
685534-36-5P 685534-38-7P 685534-39-8P
685534-42-3P 685534-43-4P 685534-46-7P
685534-47-8P, N-[5-Chloro-2-[(E)-3-[4-(4-fluorobenzyl)piperazin-1-yl]-3-oxopropenyl]phenyl]acetamide **685534-50-3P**, [5-Chloro-2-[(E)-3-[4-(4-fluorobenzyl)piperazin-1-yl]-3-oxopropenyl]phenyl]urea **685534-51-4P 685534-55-8P**
685534-57-0P 685534-58-1P 685534-59-2P
685534-61-6P 685534-62-7P 685534-68-3P
685534-69-4P 685534-70-7P 685534-75-2P
685534-76-3P 685534-82-1P 685534-83-2P

685534-90-1P 685534-92-3P 685534-94-5P
685534-95-6P 685534-96-7P 685534-97-8P
685534-99-0P 685535-04-0P 685535-11-9P
685535-13-1P 685535-18-6P 685535-20-0P
685535-27-7P 685535-28-8P 685535-29-9P
685535-30-2P 685535-37-9P 685535-38-0P
685535-39-1P 685535-40-4P 685535-41-5P
685535-42-6P 685535-45-9P 685535-46-0P
685535-48-2P 685535-51-7P 685535-52-8P
685535-53-9P 685535-54-0P 685535-59-5P
685535-61-9P 685535-63-1P 685535-65-3P
685535-67-5P 685535-70-0P 685535-72-2P
685535-74-4P 685535-76-6P 685535-78-8P
685535-80-2P 685535-82-4P 685535-83-5P
685535-84-6P 685535-85-7P, 5-Chloro-2-[(E)-3-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-3-oxopropenyl]-N-(1-methylpiperidin-4-yl)benzamide **685535-86-8P**, N-(1-Benzylpiperidin-4-yl)-5-chloro-2-[(E)-3-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-3-oxopropenyl]benzamide **685535-87-9P**, 4-[[5-Chloro-2-[(E)-3-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-3-oxopropenyl]benzoyl]amino]piperidine-1-carboxylic acid ethyl ester **685535-88-0P**
685535-89-1P 685535-91-5P 685535-93-7P
685535-95-9P, N-[5-Chloro-2-[(E)-3-[4-(4-chlorobenzyl)-2-methylpiperazin-1-yl]-3-oxopropenyl]phenyl]acetamide **685535-98-2P**, N-[5-Chloro-2-[(E)-3-[4-(3-fluorobenzyl)-2-methylpiperazin-1-yl]-3-oxopropenyl]phenyl]acetamide **685536-02-1P**, N-[5-Chloro-2-[(E)-3-[4-(2,4-difluorobenzyl)-2-methylpiperazin-1-yl]-3-oxopropenyl]phenyl]acetamide **685536-06-5P**, N-[5-Chloro-2-[(E)-3-[4-(4-cyanobenzyl)-2-methylpiperazin-1-yl]-3-oxopropenyl]phenyl]acetamide **685536-10-1P**, N-[5-Chloro-2-[(E)-3-[(R)-4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-3-oxopropenyl]-4-methoxyphenyl]acetamide
685536-16-7P 685536-19-0P 685536-23-6P
685536-27-0P 685536-31-6P 685536-33-8P
685536-37-2P 685536-41-8P 685536-48-5P
685536-50-9P 685536-54-3P 685536-56-5P
685536-58-7P 685536-62-3P 685536-66-7P
685536-70-3P 685536-79-2P 685539-57-5P
685842-01-7P
(CCR-1 antagonist; preparation of (benzylpiperazinyl)phenylpropenones as CCR-1 antagonists for treatment of inflammatory and autoimmune diseases)

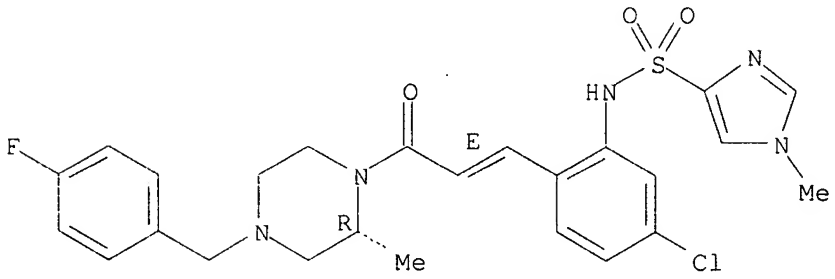
IT 685534-23-0P 685534-24-1P 685534-40-1P
685534-41-2P 685534-44-5P 685534-45-6P
685534-48-9P, [5-Chloro-2-[(E)-3-[4-(4-fluorobenzyl)piperazin-1-yl]-3-oxopropenyl]phenyl]carbamic acid tert-butyl ester
685534-49-0P 685534-54-7P 685534-66-1P
685534-67-2P 685534-73-0P 685534-74-1P
685534-80-9P 685534-81-0P 685534-88-7P
685534-89-8P 685534-91-2P 685534-93-4P
685535-26-6P 685535-31-3P 685535-34-6P
685535-35-7P 685535-36-8P 685535-49-3P
685535-50-6P
(intermediate; preparation of (benzylpiperazinyl)phenylpropenones as CCR-1 antagonists for treatment of inflammatory and autoimmune diseases)

IT 685534-27-4 685534-37-6 685534-60-5
(preparation of (benzylpiperazinyl)phenylpropenones as CCR-1 antagonists for treatment of inflammatory and autoimmune diseases)

IT 685534-33-2P
(CCR-1 antagonist; preparation of (benzylpiperazinyl)phenylpropenones as CCR-1 antagonists for treatment of inflammatory and autoimmune

diseases)
RN 685534-33-2 USPATFULL
CN Piperazine, 1-[(2E)-3-[4-chloro-2-[[(1-methyl-1H-imidazol-4-yl)sulfonyl]amino]phenyl]-1-oxo-2-propenyl]-4-[(4-fluorophenyl)methyl]-2-methyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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L50 ANSWER 1 OF 2 USPATFULL on STN
AN 2006:4554 USPATFULL
TI Cinnamide compound
IN Kimura, Teiji, Tsukuba, JAPAN
Kawano, Koki, Tsukuba, JAPAN
Doi, Eriko, Tsukuba, JAPAN
Kitazawa, Noritaka, Tsukuba, JAPAN
Shin, Kogyoku, Tsukuba, JAPAN
Miyagawa, Takehiko, Tsukuba, JAPAN
Kaneko, Toshihiko, Tsukuba, JAPAN
Ito, Koichi, Tsukuba, JAPAN
Takaishi, Mamoru, Tsukuba, JAPAN
Sasaki, Takeo, Tsukuba, JAPAN
Hagiwara, Hiroaki, Tsukuba, JAPAN
PA Eisai Co., Ltd. (non-U.S. corporation)
PI US 2006004013 A1 20060105
AI US 2005-136355 A1 20050525 (11)
PRAI JP 2004-155790 20040526
JP 2004-310909 20041026
DT Utility
FS APPLICATION
LREP BIRCH STEWART KOLASCH & BIRCH, PO BOX 747, FALLS CHURCH, VA, 22040-0747, US
CLMN Number of Claims: 37
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 18229
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to a compound represented by Formula (I): ##STR1## (wherein Ar.sub.1 represents an imidazolyl group which may be substituted with 1 to 3 substituents; Ar.sub.2 represents a pyridinyl group, a pyrimidinyl group, or a phenyl group which may be substituted with 1 to 3 substituents; X.sub.1 represents (1) --C.tbd.C-- or (2) a double bond etc. which may be substituted; R.sup.1 and R.sup.2 represent, for example, a C1-6 alkyl group or C3-8 cycloalkyl group

which may be substituted) or a pharmacologically acceptable salt thereof and to the use thereof as pharmaceutical agents. The object of the present invention is to find a therapeutic or preventive agent for diseases caused by Aβ. According to the present invention, a therapeutic or preventive agents for diseases caused by Aβ can be provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **870841-97-7P 870842-59-4P 870848-35-4P**
870848-36-5P 870848-37-6P 870848-39-8P
870848-40-1P 870848-41-2P
(preparation of cinnamide, 3-benzylidenepiperidin-2-one, phenylpropynamide compds. as amyloid β production inhibitors for treatment of neurodegenerative diseases)

L50 ANSWER 2 OF 2 USPATFULL on STN
AN 2005:221552 USPATFULL
TI Novel cinnamic amides
IN Wellner, Eric, Lund, SWEDEN
Sandin, Helena, Lund, SWEDEN
PA Active Biotech AB, Lund, SWEDEN (non-U.S. corporation)
PI US 2005192289 A1 20050901
AI US 2004-995036 A1 20041123 (10)
PRAI SE 2004-440 20040225
DT Utility
FS APPLICATION
LREP BROWDY AND NEIMARK, P.L.L.C., 624 NINTH STREET, NW, SUITE 300, WASHINGTON, DC, 20001-5303, US
CLMN Number of Claims: 15
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1449
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB E-cinnamic amides of piperazine derivatives according to formula (I) ##STR1## wherein X is chloro or fluoro and R.sup.1 is an aromatic or heteroaromatic group, their pharmaceutically acceptable salts or solvates. The invention also relates to pharmaceutical compositions containing a compound of formula (I) together with a pharmaceutically acceptable carrier. Included are also processes for the preparation of compounds of formula (I), as well as methods for treating mammals suffering from inflammatory, autoimmune, proliferative or hyperproliferative diseases by administering a compound having the formula (I) to said mammal.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **863202-77-1P 863202-83-9P**
(drug candidate; cinnamic amides, preparation, and pharmaceutical compns.)

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FILE LAST UPDATED: 8 Jan 2008 (20080108/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

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L46 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:370911 HCAPLUS
DN 140:391295
TI Preparation of 1-(4-benzylpiperazin-1-yl)-3-phenylpropenones as chemokine receptor 1 antagonists for treatment of inflammatory and autoimmune diseases
IN **Bollbuck, Birgit; Eder, Joerg; Heng, Richard ; Revesz, Laszlo; Schlapbach, Achim; Waelchli, Rudolf**
PA **Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.**
SO PCT Int. Appl., 163 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

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	WO 2004037796	A3	20040617		
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	RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
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	IN 2005CN00709	A	20070810	IN 2005-CN709	20050404 <--
	MX 2005PA04348	A	20050802	MX 2005-PA4348	20050421 <--
	US 2006173004	A1	20060803	US 2005-532331	20050422 <--
	NO 2005002487	A	20050524	NO 2005-2487	20050422 <--
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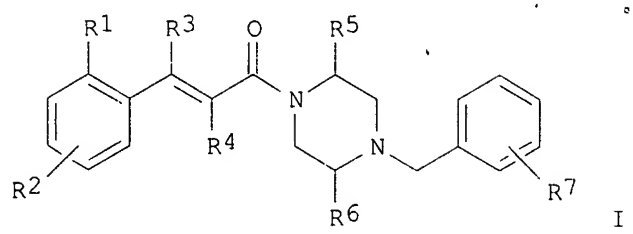

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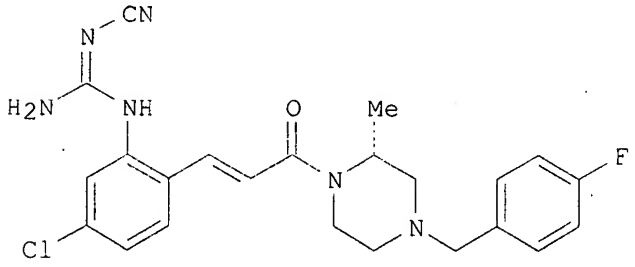

II

AB Title compds. I [wherein R1 = XR10, X(R10)2, or NR11R12; X = a linker comprising 1-4 (un)substituted N, C, O, and/or S atoms; R2 and R7 = independently H, CN, halo, NO2, or (un)substituted OH, CHO, SH, NH2, (cyclo)alkyl, alkenyl, alkynyl, heterocyclyl, or (hetero)aryl; R3 and R4 = independently H, CN, halo, (cyclo)alkyl, alkenyl, alkynyl, CO, heterocyclyl, or aryl; R5 and R6 = independently H, CN, (cyclo)alkyl, alkenyl, alkynyl, CO, heterocyclyl, or aryl; R10 = H, CN, halo, NO2, or (un)substituted OH, CHO, SH, NH2, alkyl, alkenyl, or alkynyl; NR11R12 = (un)substituted heterocyclyl or heteroaryl; and pharmaceutically acceptable salts or esters thereof] were prepared as chemokine receptor 1 (CCR-1) antagonists. For example, N-protection of (E)-3-(2-amino-4-chlorophenyl)acrylic acid Me ester with (BOC)2O in THF (94%), followed by saponification using NaOH in MeOH gave (E)-3-(2-tert-butoxycarbonylamino-4-chlorophenyl)acrylic acid (87%). Condensation of the acid with (R)-1-(4-fluorobenzyl)-3-methylpiperazine provided the amide (81%). Deprotection with concentrate HCl in EtOH afforded the amine (80%), which was refluxed with NaN(CN)2 in ethoxyethanol and 2N HCl to give the guanidine II (30%). Compds. of the invention demonstrated inhibition of binding of MIP1α to the human CCR-1 receptor with IC50 values ranging from 0.1 nM to 1000 nM and inhibition of Ca2+ mobilization in response to MIP1α with IC50 values ranging from 0.1 nM to 1000 nM. Thus, I and their pharmaceutical compns. are useful for treatment of diseases and conditions in which CCR-1 is implicated, e.g. inflammatory and autoimmune diseases (no data).

IT **685534-33-2P 685534-35-4P 685534-56-9P**
685535-44-8P 685535-79-9P 685535-81-3P
685536-74-7P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(CCR-1 antagonist; preparation of (benzylpiperazinyl)phenylpropenones as CCR-1 antagonists for treatment of inflammatory and autoimmune diseases)

IT **685534-20-7P 685534-25-2P 685534-26-3P**
685534-28-5P 685534-29-6P 685534-30-9P

685534-31-0P 685534-32-1P 685534-34-3P
685534-36-5P 685534-38-7P 685534-39-8P
685534-42-3P 685534-43-4P 685534-46-7P
685534-47-8P, N-[5-Chloro-2-[(E)-3-[4-(4-fluorobenzyl)piperazin-1-yl]-3-oxopropenyl]phenyl]acetamide 685534-50-3P, [5-Chloro-2-[(E)-3-[4-(4-fluorobenzyl)piperazin-1-yl]-3-oxopropenyl]phenyl]urea 685534-51-4P 685534-55-8P
685534-57-0P 685534-58-1P 685534-59-2P
685534-61-6P 685534-62-7P 685534-68-3P
685534-69-4P 685534-70-7P 685534-75-2P
685534-76-3P 685534-82-1P 685534-83-2P
685534-90-1P 685534-92-3P 685534-94-5P
685534-95-6P 685534-96-7P 685534-97-8P
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685535-13-1P 685535-18-6P 685535-20-0P
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685535-30-2P 685535-37-9P 685535-38-0P
685535-39-1P 685535-40-4P 685535-41-5P
685535-42-6P 685535-45-9P 685535-46-0P
685535-48-2P 685535-51-7P 685535-52-8P
685535-53-9P 685535-54-0P 685535-59-5P
685535-61-9P 685535-63-1P 685535-65-3P
685535-67-5P 685535-70-0P 685535-72-2P
685535-74-4P 685535-76-6P 685535-78-8P
685535-80-2P 685535-82-4P 685535-83-5P
685535-84-6P 685535-85-7P, 5-Chloro-2-[(E)-3-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-3-oxopropenyl]-N-(1-methylpiperidin-4-yl)benzamide 685535-86-8P, N-(1-Benzylpiperidin-4-yl)-5-chloro-2-[(E)-3-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-3-oxopropenyl]benzamide 685535-87-9P, 4-[[5-Chloro-2-[(E)-3-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-3-oxopropenyl]benzoyl]amino]piperidine-1-carboxylic acid ethyl ester 685535-88-0P
685535-89-1P 685535-91-5P 685535-93-7P
685535-95-9P, N-[5-Chloro-2-[(E)-3-[4-(4-chlorobenzyl)-2-methylpiperazin-1-yl]-3-oxopropenyl]phenyl]acetamide 685535-98-2P , N-[5-Chloro-2-[(E)-3-[4-(3-fluorobenzyl)-2-methylpiperazin-1-yl]-3-oxopropenyl]phenyl]acetamide 685536-02-1P, N-[5-Chloro-2-[(E)-3-[4-(2,4-difluorobenzyl)-2-methylpiperazin-1-yl]-3-oxopropenyl]phenyl]acetamide 685536-06-5P, N-[5-Chloro-2-[(E)-3-[4-(4-cyanobenzyl)-2-methylpiperazin-1-yl]-3-oxopropenyl]phenyl]acetamide 685536-10-1P, N-[5-Chloro-2-[(E)-3-[(R)-4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-3-oxopropenyl]-4-methoxyphenyl]acetamide
685536-16-7P 685536-19-0P 685536-23-6P
685536-27-0P 685536-31-6P 685536-33-8P
685536-37-2P 685536-41-8P 685536-48-5P
685536-50-9P 685536-54-3P 685536-56-5P
685536-58-7P 685536-62-3P 685536-66-7P
685536-70-3P 685536-79-2P 685539-57-5P
685842-01-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(CCR-1 antagonist; preparation of (benzylpiperazinyl)phenylpropenones as CCR-1 antagonists for treatment of inflammatory and autoimmune diseases)

IT 685534-23-0P 685534-24-1P 685534-40-1P
685534-41-2P 685534-44-5P 685534-45-6P
685534-48-9P, [5-Chloro-2-[(E)-3-[4-(4-fluorobenzyl)piperazin-1-yl]-3-oxopropenyl]phenyl]carbamic acid tert-butyl ester
685534-49-0P 685534-54-7P 685534-66-1P

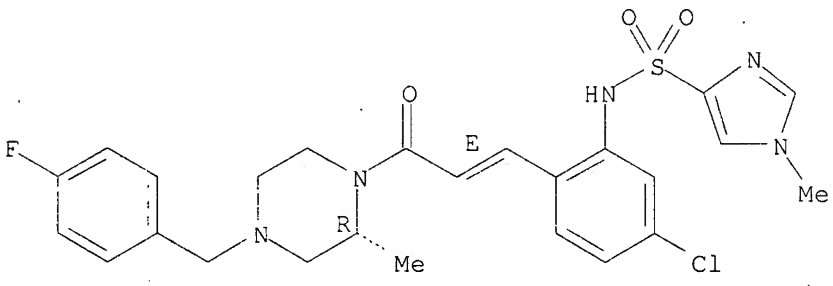
685534-67-2P 685534-73-0P 685534-74-1P
685534-80-9P 685534-81-0P 685534-88-7P
685534-89-8P 685534-91-2P 685534-93-4P
685535-26-6P 685535-31-3P 685535-34-6P
685535-35-7P 685535-36-8P 685535-49-3P
685535-50-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of (benzylpiperazinyl)phenylpropenones as CCR-1 antagonists for treatment of inflammatory and autoimmune diseases)

IT **685534-27-4 685534-37-6 685534-60-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of (benzylpiperazinyl)phenylpropenones as CCR-1 antagonists for treatment of inflammatory and autoimmune diseases)

IT **685534-33-2P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(CCR-1 antagonist; preparation of (benzylpiperazinyl)phenylpropenones as CCR-1 antagonists for treatment of inflammatory and autoimmune diseases)

RN 685534-33-2 HCAPLUS
CN Piperazine, 1-[(2E)-3-[4-chloro-2-[[(1-methyl-1H-imidazol-4-yl)sulfonyl]amino]phenyl]-1-oxo-2-propenyl]-4-[(4-fluorophenyl)methyl]-2-methyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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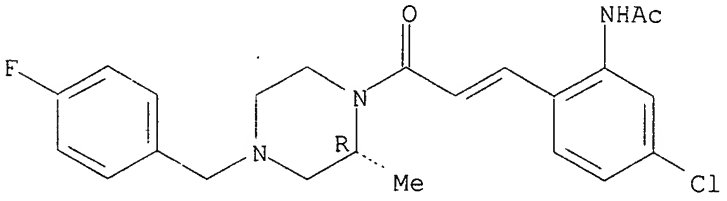
L47 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2008 ACS on STN
AN 2006:1199252 HCAPLUS
DN 146:176166
TI Bridged piperazines and piperidines as CCR1 antagonists with oral activity in models of arthritis and multiple sclerosis
AU **Revesz, Laszlo**; **Bollbuck, Birgit**; Buhl, Thomas; Dawson, Janet; Feifel, Roland; **Heng, Richard**; Hiestand, Peter; Sparrer, Helmut; **Schlapbach, Achim**; **Waelchli, Rudolf**; Loetscher, Pius
CS Global Discovery Chemistry, **Novartis** Institutes for BioMedical Research, Basel, CH-4002, Switz.
SO Letters in Drug Design & Discovery (2006), 3(10), 689-694
CODEN: LDDDAW; ISSN: 1570-1808
PB Bentham Science Publishers Ltd.
DT Journal

LA English
AB CCR1 antagonists were prepared by coupling bridged piperazines and bridged piperidines with 2-acetylamino-4-chloro-5-methoxy cinnamic acid. Compound 2 of the series showed the desired equal potency against human, mouse and rat CCR1 (IC50 = 20; 22; 28nM), exhibited a superior pharmacokinetic profile and inhibited the clin. grades in rat acute exptl. autoimmune encephalomyelitis and knee swelling in rat antigen induced arthritis at doses of 2+30 and 2+15 mg/kg p.o.
IT **921208-31-3**
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bridged piperazines and piperidines as CCR1 antagonists with oral activity in models of arthritis and multiple sclerosis)
IT **921208-31-3**
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bridged piperazines and piperidines as CCR1 antagonists with oral activity in models of arthritis and multiple sclerosis)
RN 921208-31-3 HCAPLUS
CN Acetamide, N-[5-chloro-2-[3-[(2R)-4-[(4-fluorophenyl)methyl]-2-methyl-1-piperazinyl]-3-oxo-1-propen-1-yl]phenyl]- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



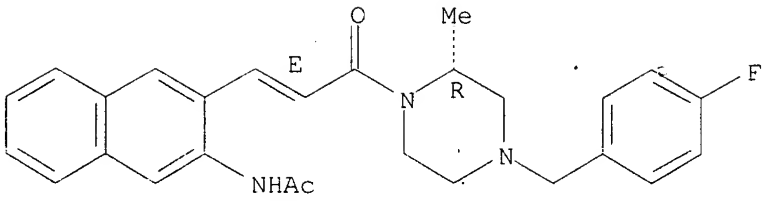
RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Arjunan, P	1981	46	3196	J Org Chem	HCAPLUS
Blumberg, L				WO 2004009588	HCAPLUS
Godessart, N	2001	13	670	Curr Opin Immunol	HCAPLUS
Godiska, R	1995	58	167	J Neuroimmunol	HCAPLUS
Horuk, R	2001	76	193	Immunol Lett	HCAPLUS
Horuk, R	2001	276	4199	J Biol Chem	HCAPLUS
Karpus, W	1997	62	691	J Leukocyte Biol	
Loetscher, P	2002	4	233	Arthritis Res	
Lowe, J	1994	37	2831	J Med Chem	HCAPLUS
Ninichuk, V	2005	25	365	Am J Nephrol	HCAPLUS
Pease, J	2005	14	785	Expert Opin Invest D	HCAPLUS
Revesz, L	2005	46	5577	Tetrahedron Lett	HCAPLUS

L47 ANSWER 2 OF 2 HCAPLUS • COPYRIGHT 2008 ACS on STN
AN 2005:1144476 HCAPLUS
DN 144:51547
TI Novel CCR1 antagonists with oral activity in the mouse collagen induced arthritis
AU **Revesz, Laszlo; Bollbuck, Birgit**; Buhl, Thomas; **Eder, Joerg**; Esser, Ronald; Feifel, Roland; **Heng, Richard**; Hiestand, Peter; Jachez-Demange, Benedicte; Loetscher, Pius; Sparrer, Helmut; **Schlapbach, Achim; Waelchli, Rudolf**

CS **Novartis** Institutes for BioMedical Research, Global Discovery Chemistry, Autoimmunity and Transplantation, Basel, CH-4002, Switz.
SO Bioorganic & Medicinal Chemistry Letters (2005), 15(23), 5160-5164 CODEN: BMCLE8; ISSN: 0960-894X.
PB Elsevier B.V.
DT Journal
LA English
OS CASREACT 144:51547
AB Cinnamides as novel CCR1 antagonist chemotypes are described with high affinity to human and rodent receptors. Two compds., (2R)-1-[3-[2-[(aminocarbonyl)amino]-4-chlorophenyl]-1-oxo-2-propenyl]-4-[(4-fluorophenyl)methyl]-2-(methyl)piperazine and N-[5-chloro-2-[3-[3-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]octyl]-3-oxo-1-propenyl]phenyl]-2-(dimethylamino)acetamide, showed oral activity in the mouse collagen induced arthritis.
IT **685534-62-7P 685534-76-3P 871324-93-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of [(fluorophenyl)methyl]piperazine derivs. and study of their activity as orally active CCR1 antagonists in collagen-induced arthritis)
IT **685534-24-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of [(fluorophenyl)methyl]piperazine derivs. and study of their activity as orally active CCR1 antagonists in collagen-induced arthritis model)
IT **685534-25-2P 685534-42-3P 685534-43-4P 685534-47-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of [[[chloro(acetylamino)phenoxy]methyl]carbonyl](fluorobenzyl) piperazine derivs. and study of their activity as orally active CCR1 antagonists in collagen-induced arthritis)
IT **685534-28-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of [chloro[(fluorobenzyl)(methyl)piperazinyl]oxopropenyl]phenyl]urea derivative and study of its activity as orally active CCR1 antagonist in collagen-induced arthritis)
IT **685534-62-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of [(fluorophenyl)methyl]piperazine derivs. and study of their activity as orally active CCR1 antagonists in collagen-induced arthritis)
RN 685534-62-7 HCAPLUS
CN Acetamide, N-[3-[(1E)-3-[(2R)-4-[(4-fluorophenyl)methyl]-2-methyl-1-piperazinyl]-3-oxo-1-propenyl]-2-naphthalenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Akira, N	2001	26	121	Drugs Future	
Blumberg, L	2002			WO 2002032901	HCAPLUS
Bollbuck, B	2004			WO 2004037796	HCAPLUS
Bolos, J	1996	39	2962	J Med Chem	HCAPLUS
Brown, M	2004	14	2175	Bioorg Med Chem Lett	HCAPLUS
Gladue, R	2003	278	40473	J Biol Chem	HCAPLUS
Godessart, N	2001	13	670	Curr Opin Immunol	HCAPLUS
Godiska, R	1995	58	167	J Neuroimmunol	HCAPLUS
Haringman, J	2003	62	715	Ann Rheum Dis	HCAPLUS
Hesselgesser, J	1998	273	15687	J Biol Chem	HCAPLUS
Hilger, C	2002			WO 2002036581	HCAPLUS
Horuk, R	2001	76	193	Immunol Lett	HCAPLUS
Horuk, R	2001	76	193	Immunol Lett	HCAPLUS
Horuk, R	2001	276	4199	J Biol Chem	HCAPLUS
Horuk, R	2001	276	4199	J Biol Chem	HCAPLUS
Karpus, W	1997	62	691	J Leukocyte Biol	
Kath, J	2004	14	2163	Bioorg Med Chem Lett	HCAPLUS
Kath, J	2004	14	2169	Bioorg Med Chem Lett	HCAPLUS
Katti, H	1983	22	1205	Ind J Chem Section B	
Kori, M	2002			WO 2001098282 A1	HCAPLUS
Liang, M	2000	275	19000	J Biol Chem	HCAPLUS
Loetscher, P	2002	4	233	Arthritis Res	
Mavunkel, B	2001			WO 2000071535	HCAPLUS
Naya, A	2001	44	1429	J Med Chem	HCAPLUS
Ng, H	1999	42	4680	J Med Chem	HCAPLUS
Pennell, A	2004			WO 2003105853	HCAPLUS
Smith, D	1991			EP 345808	HCAPLUS

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(FILE 'HOME' ENTERED AT 14:02:02 ON 10 JAN 2008)
SET COST OFF

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L2 13 S E4,E5
E EDER/AU
L3 2 S E3
E EDER J/AU
L4 207 S E3-E7,E15,E19
E HENG/AU
E HENG R/AU
L5 21 S E3,E4
E REVESZ/AU

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                E REVESZ L/AU
L6          157 S E3-E5
                E SCHLAPBACH/AU
L7           23 S E4,E5
                E WALCHLI/AU
L8            2 S E20
                E NOVARTIS/CO
                E E5+ALL
L9        74857 S E2+RT OR E2-E211/PA,CS
                E NOVART/CO
L10        6623 S E4-E6/PA,CS,CO
                E NOVAR/CO
L11           1 S E11/PA,CS,CO
L12           3 S E14-E19,E23,E24/PA,CS,CW

     FILE 'REGISTRY' ENTERED AT 14:06:10 ON 10 JAN 2008

     FILE 'HCAPLUS' ENTERED AT 14:06:10 ON 10 JAN 2008
L13             TRA L1 1- RN :      265 TERMS

     FILE 'REGISTRY' ENTERED AT 14:06:10 ON 10 JAN 2008
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L16            50 S L15
L17               STR L15
L18            42 S L17
L19               STR L17
L20            20 S L19
L21           398 S L19 FUL
                  SAV TEMP L21 SACKEY532A/A
L22           141 S L14 AND L21
L23               STR L19
L24               STR L23
L25             7 S L24 SAM SUB=L21
L26           148 S L24 FUL SUB=L21
                  SAV TEMP L26 SACKEY532B/A
L27           134 S L26 AND L22
L28             7 S L22 NOT L27
L29             1 S NCNC2-C5/ES AND L21
L30             1 S NCNC2-C6/ES AND L21
L31            17 S NCNC2/ES AND L21
L32            10 S L31 NOT L27-L30
L33           151 S L27-L32
L34            14 S L26 NOT L33
L35           165 S L26,L33,L34
L36            17 S L35 NOT L26
L37             7 S L36 AND L14
L38           165 S L35,L37

     FILE 'HCAPLUS' ENTERED AT 14:20:02 ON 10 JAN 2008
L39             7 S L38
L40             3 S L39 AND L1-L12
                E WAELCHLI/AU
L41            31 S E26,E27,E29,E30
L42             3 S L39 AND L41
L43             3 S L40,L42
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L45             1 S L39 AND (PD<=20021025 OR PRD<=20021025 OR AD<=20021025) AND P
L46             1 S L45 AND L39-L45
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L50             2 S L48 NOT L49

     FILE 'REGISTRY' ENTERED AT 14:23:39 ON 10 JAN 2008

     FILE 'USPATFULL' ENTERED AT 14:23:50 ON 10 JAN 2008

     FILE 'HCAPLUS' ENTERED AT 14:24:13 ON 10 JAN 2008

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STIC
Scientific & Technical Information Center

Search Report
EIC 1700

STIC Database Tracking Number: 24[illegible]

To: EBENEZER SACKEY Location: REM-5B31 / Mailbox 5C18 Art Unit: 1624 Monday, November 26, 2007 Phone: (571) 272-0704 Case Serial Number: 10 / 532331	From: JAN DELAVAL Location: EIC1700 REM-4B28 / REM-4A30 Phone: (571) 272-2504 jan.delaval@uspto.gov

Search Notes

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Search and Information Resources Administration

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SCIENTIFIC REFERENCE BR
Tech Info

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Pat. & T.M Office

ACCESS DB # 243399

PLEASE PRINT CLEARLY

Scientific and Technical Information Center

SEARCH REQUEST FORM

Requester's Full Name: BEN SACKEY Examiner #: 73489 Date: 11/19/07

Art Unit: 1624 Phone Number: 2-0704 Serial Number: 10/532,331

Location (Bldg/Room#): Rem 5B3 (Mailbox #): 5C18 Results Format Preferred (circle): PAPER DISK

****

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

Title of Invention: 1-(4-Benzyl-piperazin-1-yl)-3-phenyl-propenone der.

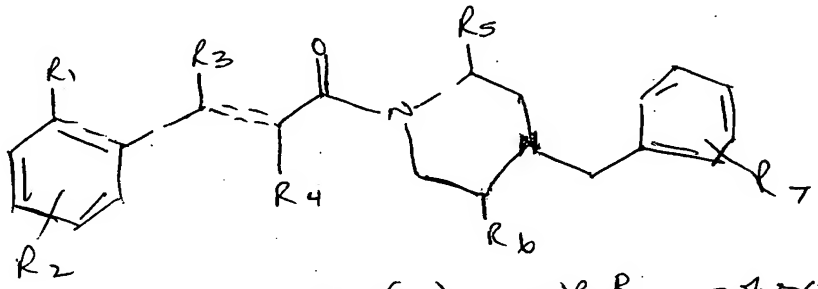
Inventors (please provide full names): Bollbuck et al.

Earliest Priority Date: 1 or 1 24/03

Search Topic:

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known.

For Sequence Searches Only ***Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.***



(1)

where R_1 is $X-R_{10}$, $X-(R_{10})_2$ or $NR_{11}R_{12}$ where X, R_{10}, R_{11} and R_{12} are as defined.

R_2 and R_7, R_3 and R_4, R_5 and R_6 are as defined.

please note formulae (II), (IIa) and (III).

Thanks

****

STAFF USE ONLY

Searcher: Ja

Searcher Phone #:

Searcher Location:

Date Searcher Picked Up: 11/26/07

Date Completed: 11/26/07

Searcher Prep & Review Time: 20

Online Time: +40

Type of Search

___ NA Sequence (#)

___ AA Sequence (#)

✓ Structure (#)

___ Bibliographic

___ Litigation

___ Fulltext

___ Other

Vendors and cost where applicable

✓ STN ___ Dialog

___ Questel/Orbit ___ Lexis/Nexis

___ Westlaw ___ WWW/Internet

___ In-house sequence systems

___ Commercial ___ Oligomer ___ Score/Length

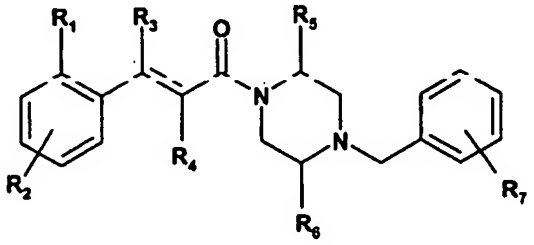
___ Interference ___ SPDI ___ Encode/Transl

___ Other (specify)

10/532,331

Amendments to the Claims:

1. (currently amended) A compound of formula I, or a pharmaceutically acceptable salt or ester thereof,



Ben - I looked in eDan at the Spec - I interpret this yellow area as a double bond " C = C "

wherein

R_1 is -X-R_{10}, -X-$(R_{10})_2$ or $-NR_{11}R_{12}$

Wherein X is a linker comprising 1 atom or a chain comprising 2, 3 or 4 atoms selected from N, C, O or S, and wherein when said linker comprises 2 or more C atoms the linker may comprise 1 or more C=C or C≡C bonds;

wherein any of said atoms has up to 2 optional substituents selected from hydrogen, oxo, cyano, halo, nitro or optionally substituted oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, sulfur amino;

R_{10} is a substituent independently selected from the group consisting of hydrogen, cyano, halo, nitro or optionally substituted oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, amino, cycloalkyl, heterocycloalkyl, aryl, heteroaryl;

R_{11} and R_{12} each represent a lower alkyl group connected together such that R_1 is an optionally substituted heterocycloalkyl or heteroaryl group;

R_2 and R_7 represent one or more substituents attached to the phenyl ring selected from the group consisting of hydrogen, cyano, halo, nitro or optionally substituted oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, amino, sulfur, cycloalkyl, heterocycloalkyl, aryl, heteroaryl or a substituent forming a bicyclic ring system of which the phenyl ring to which it is attached forms part of the bicycle for example butadiene forming napthyl, or heterobutadiene forming quinolinyl, quinoxalinyl or isoquinolinyl;

R_3 and R_4 are independently selected from the group consisting of hydrogen, cyano, halo, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, cycloalkyl, heterocycloalkyl, aryl;

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provided by InfoChem.

STRUCTURE FILE UPDATES:   25 NOV 2007  HIGHEST RN 955919-54-7
DICTIONARY FILE UPDATES:  25 NOV 2007  HIGHEST RN 955919-54-7

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TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

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L17             STR
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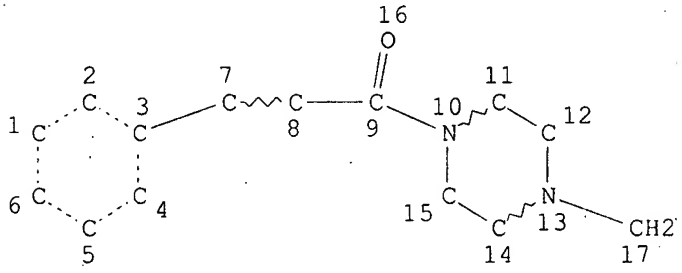

Search report sent to SCORE

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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  23

STEREO ATTRIBUTES: NONE
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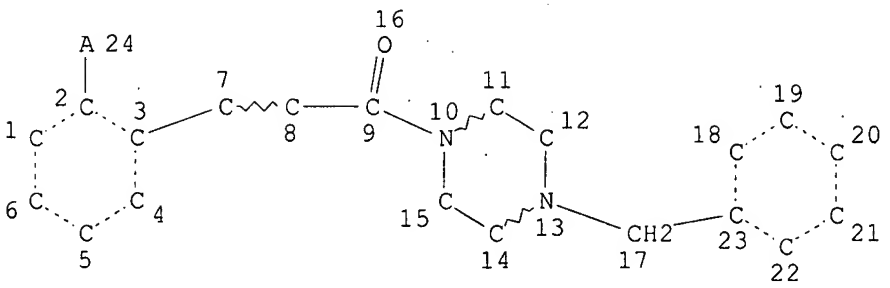

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		E	E5+ALL
L2	74401	S	E26+RT OR E26-E225/PA,CS
		E	NOVARTI/CO
L3	6538	S	E229 OR NOVARTIS?/PA,CS,CO
		E	BOLLBUCK/AU
L4	13	S	E241,E242
		E	EDER/AU
L5	45	S	E3
		E	EDER J/AU
L6	198	S	E264-E268,E276,E280
		E	HENG/AU
		E	HENG R/AU
L7	21	S	E444,E445
		E	REVESZ/AU
		E	REVESZ L/AU
L8	157	S	E468-E470
		E	REVES/AU
		E	REVEZ/AU
		E	SCHLAPBACH/AU
L9	22	S	E505,E506
		E	WALCHLI/AU
L10	2	S	E533

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                E WAELCHLI/AU
L11          26 S E563,E563,E566,E567
L12           1 S L1 AND L2-L11

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     FILE 'HCAPLUS' ENTERED AT 07:08:53 ON 26 NOV 2007
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L16           50 S L15
L17              STR L15
L18           50 S L17
L19         2323 S L17 FUL
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L20          141 S L14 AND L19
L21              STR L17
L22           23 S L21 SAM SUB=L19
L23              STR L21
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L46           16 S L43-L45
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                 SEL HIT RN L46

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L56         2246 SEA L55
L57           17 S L56 AND L26

     FILE 'REGISTRY' ENTERED AT 07:36:48 ON 26 NOV 2007

=> fil uspatful
FILE 'USPATFULL' ENTERED AT 07:37:09 ON 26 NOV 2007
CA INDEXING COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 22 Nov 2007 (20071122/PD)
FILE LAST UPDATED: 22 Nov 2007 (20071122/ED)
HIGHEST GRANTED PATENT NUMBER: US7299504
HIGHEST APPLICATION PUBLICATION NUMBER: US2007271667
CA INDEXING IS CURRENT THROUGH 22 Nov 2007 (20071122/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 22 Nov 2007 (20071122/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Oct 2007
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Oct 2007


=> d l38 bib abs hitrn fhitstr

L38  ANSWER 1 OF 1  USPATFULL on STN
AN     2006:203118  USPATFULL
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IN     Bollbuck, Birgit, Weil am Rhein, GERMANY, FEDERAL REPUBLIC OF
       Eder, Jorg, Rheinfelden, GERMANY, FEDERAL REPUBLIC OF
       Heng, Richard, Hegenheim, FRANCE
       Revesz, Laszlo, Therwil, SWITZERLAND
       Schlapbach, Achim, Lorrach, GERMANY, FEDERAL REPUBLIC OF
       Walchli, Rudolf, Basel, SWITZERLAND
PI     US 2006173004       A1  20060803
AI     US 2003-532331      A1  20031024 (10)
       WO 2003-EP11848         20031024
                               20050422  PCT 371 date
PRAI   GB 2002-24917       20021025
DT     Utility
FS     APPLICATION
LREP   NOVARTIS, CORPORATE INTELLECTUAL PROPERTY, ONE HEALTH PLAZA 104/3, EAST
       HANOVER, NJ, 07936-1080, US
CLMN   Number of Claims: 9
ECL    Exemplary Claim: 1
DRWN   No Drawings
LN.CNT 4060
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB     A compound of formula (I), or a pharmaceutically acceptable salt or
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ester thereof, wherein the symbols have meaning as defined, which are antagonists of CCR-1 and which find use pharmaceutically for treatment of diseases and conditions in which CCR-1 is implicated, e.g. inflammatory diseases. ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT **685534-33-2P 685534-35-4P 685534-56-9P 685535-44-8P 685535-79-9P 685535-81-3P 685536-74-7P**
(CCR-1 antagonist; preparation of (benzylpiperazinyl)phenylpropenones as CCR-1 antagonists for treatment of inflammatory and autoimmune diseases)

IT **685534-20-7P 685534-25-2P 685534-26-3P 685534-28-5P 685534-29-6P 685534-30-9P 685534-31-0P 685534-32-1P 685534-34-3P 685534-36-5P 685534-38-7P 685534-39-8P 685534-42-3P 685534-43-4P 685534-46-7P 685534-47-8P**, N-[5-Chloro-2-[(E)-3-[4-(4-fluorobenzyl)piperazin-1-yl]-3-oxopropenyl]phenyl]acetamide **685534-50-3P**, [5-Chloro-2-[(E)-3-[4-(4-fluorobenzyl)piperazin-1-yl]-3-oxopropenyl]phenyl]urea **685534-51-4P 685534-55-8P 685534-57-0P 685534-58-1P 685534-59-2P 685534-61-6P 685534-62-7P 685534-68-3P 685534-69-4P 685534-70-7P 685534-75-2P 685534-76-3P 685534-82-1P 685534-83-2P 685534-90-1P 685534-92-3P 685534-94-5P 685534-95-6P 685534-96-7P 685534-97-8P 685534-99-0P 685535-04-0P 685535-11-9P 685535-13-1P 685535-18-6P 685535-20-0P 685535-27-7P 685535-28-8P 685535-29-9P 685535-30-2P 685535-37-9P 685535-38-0P 685535-39-1P 685535-40-4P 685535-41-5P 685535-42-6P 685535-45-9P 685535-46-0P 685535-48-2P 685535-51-7P 685535-52-8P 685535-53-9P 685535-54-0P 685535-59-5P 685535-61-9P 685535-63-1P 685535-65-3P 685535-67-5P 685535-70-0P 685535-72-2P 685535-74-4P 685535-76-6P 685535-78-8P 685535-80-2P 685535-82-4P 685535-83-5P 685535-84-6P 685535-85-7P**, 5-Chloro-2-[(E)-3-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-3-oxopropenyl]-N-(1-methylpiperidin-4-yl)benzamide **685535-86-8P**, N-(1-Benzylpiperidin-4-yl)-5-chloro-2-[(E)-3-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-3-oxopropenyl]benzamide **685535-87-9P**, 4-[[5-Chloro-2-[(E)-3-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-3-oxopropenyl]benzoyl]amino]piperidine-1-carboxylic acid ethyl ester **685535-88-0P 685535-89-1P 685535-91-5P 685535-93-7P 685535-95-9P**, N-[5-Chloro-2-[(E)-3-[4-(4-chlorobenzyl)-2-methylpiperazin-1-yl]-3-oxopropenyl]phenyl]acetamide **685535-98-2P**, N-[5-Chloro-2-[(E)-3-[4-(3-fluorobenzyl)-2-methylpiperazin-1-yl]-3-oxopropenyl]phenyl]acetamide **685536-02-1P**, N-[5-Chloro-2-[(E)-3-[4-(2,4-difluorobenzyl)-2-methylpiperazin-1-yl]-3-oxopropenyl]phenyl]acetamide **685536-06-5P**, N-[5-Chloro-2-[(E)-3-[4-(4-cyanobenzyl)-2-methylpiperazin-1-yl]-3-oxopropenyl]phenyl]acetamide **685536-10-1P**, N-[5-Chloro-2-[(E)-3-[(R)-4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-3-oxopropenyl]-4-methoxyphenyl]acetamide **685536-16-7P 685536-19-0P 685536-23-6P 685536-27-0P 685536-31-6P 685536-33-8P 685536-37-2P 685536-41-8P 685536-48-5P 685536-50-9P 685536-54-3P 685536-56-5P**

685536-58-7P 685536-62-3P 685536-66-7P
685536-70-3P 685536-79-2P 685539-57-5P
685842-01-7P
(CCR-1 antagonist; preparation of (benzylpiperazinyl)phenylpropenones as CCR-1 antagonists for treatment of inflammatory and autoimmune diseases)

IT 685534-23-0P 685534-24-1P 685534-40-1P
685534-41-2P 685534-44-5P 685534-45-6P
685534-48-9P, [5-Chloro-2-[(E)-3-[4-(4-fluorobenzyl)piperazin-1-yl]-3-oxopropenyl]phenyl]carbamic acid tert-butyl ester
685534-49-0P 685534-54-7P 685534-66-1P
685534-67-2P 685534-73-0P 685534-74-1P
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685534-89-8P 685534-91-2P 685534-93-4P
685535-26-6P 685535-31-3P 685535-34-6P
685535-35-7P 685535-36-8P 685535-49-3P
685535-50-6P
(intermediate; preparation of (benzylpiperazinyl)phenylpropenones as CCR-1 antagonists for treatment of inflammatory and autoimmune diseases)

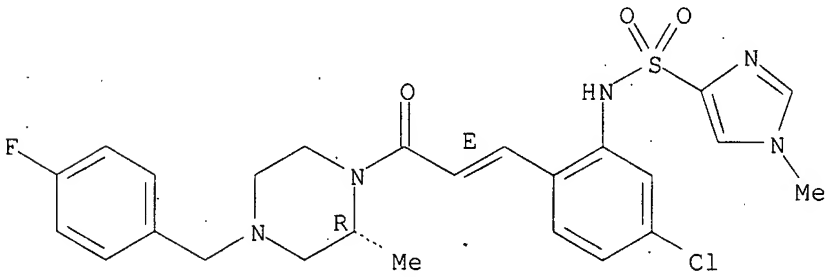
IT 685534-27-4 685534-37-6 685534-60-5
(preparation of (benzylpiperazinyl)phenylpropenones as CCR-1 antagonists for treatment of inflammatory and autoimmune diseases)

IT 685534-33-2P
(CCR-1 antagonist; preparation of (benzylpiperazinyl)phenylpropenones as CCR-1 antagonists for treatment of inflammatory and autoimmune diseases)

RN 685534-33-2 USPATFULL

CN Piperazine, 1-[(2E)-3-[4-chloro-2-[[(1-methyl-1H-imidazol-4-yl)sulfonyl]amino]phenyl]-1-oxo-2-propenyl]-4-[(4-fluorophenyl)methyl]-2-methyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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FILE COVERS 1907 - 26 Nov 2007 VOL 147 ISS 23
FILE LAST UPDATED: 25 Nov 2007 (20071125/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

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L36 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:370911 HCAPLUS
DN 140:391295
TI Preparation of 1-(4-benzylpiperazin-1-yl)-3-phenylpropenones as chemokine receptor 1 antagonists for treatment of inflammatory and autoimmune diseases
IN **Bollbuck, Birgit; Eder, Joerg; Heng, Richard ; Revesz, Laszlo; Schlapbach, Achim; Waelchli, Rudolf**
PA **Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.**
SO PCT Int. Appl., 163 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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	RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
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	AU 2003296559	A1	20040513	AU 2003-296559	20031024 <--
	EP 1558594	A2	20050803	EP 2003-809328	20031024 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
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	IN 2005CN00709	A	20070810	IN 2005-CN709	20050421 <--
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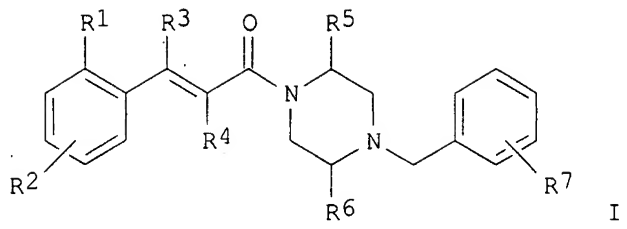

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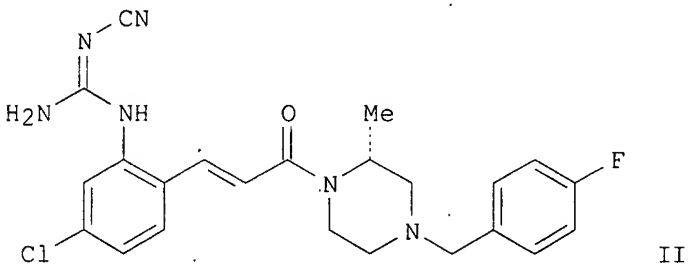

II

AB Title compds. I [wherein R1 = XR10, X(R10)2, or NR11R12; X = a linker comprising 1-4 (un)substituted N, C, O, and/or S atoms; R2 and R7 = independently H, CN, halo, NO2, or (un)substituted OH, CHO, SH, NH2, (cyclo)alkyl, alkenyl, alkynyl, heterocyclyl, or (hetero)aryl; R3 and R4 = independently H, CN, halo, (cyclo)alkyl, alkenyl, alkynyl, CO, heterocyclyl, or aryl; R5 and R6 = independently H, CN, (cyclo)alkyl, alkenyl, alkynyl, CO, heterocyclyl, or aryl; R10 = H, CN, halo, NO2, or (un)substituted OH, CHO, SH, NH2, alkyl, alkenyl, or alkynyl; NR11R12 = (un)substituted heterocyclyl or heteroaryl; and pharmaceutically acceptable salts or esters thereof] were prepared as chemokine receptor 1 (CCR-1) antagonists. For example, N-protection of (E)-3-(2-amino-4-chlorophenyl)acrylic acid Me ester with (BOC)2O in THF (94%), followed by saponification using NaOH in MeOH gave (E)-3-(2-tert-butoxycarbonylamino-4-chlorophenyl)acrylic acid (87%). Condensation of the acid with (R)-1-(4-fluorobenzyl)-3-methylpiperazine provided the amide (81%). Deprotection with concentrate HCl in EtOH afforded the amine (80%), which was refluxed with NaN(CN)2 in ethoxyethanol and 2N HCl to give the guanidine II (30%). Compds. of the invention demonstrated inhibition of binding of MIP1α to the human CCR-1 receptor with IC50 values ranging from 0.1 nM to 1000 nM and inhibition of Ca2+ mobilization in response to MIP1α with IC50 values ranging from 0.1 nM to 1000 nM. Thus, I and their pharmaceutical compns. are useful for treatment of diseases and conditions in which CCR-1 is implicated, e.g. inflammatory and autoimmune diseases (no data).

IT **685534-33-2P 685534-35-4P 685534-56-9P 685535-44-8P 685535-79-9P 685535-81-3P 685536-74-7P**

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(CCR-1 antagonist; preparation of (benzylpiperazinyl)phenylpropenones as CCR-1 antagonists for treatment of inflammatory and autoimmune diseases)

IT **685534-20-7P 685534-25-2P 685534-26-3P 685534-28-5P 685534-29-6P 685534-30-9P 685534-31-0P 685534-32-1P 685534-34-3P 685534-36-5P 685534-38-7P 685534-39-8P**

685534-42-3P 685534-43-4P 685534-46-7P
685534-47-8P, N-[5-Chloro-2-[(E)-3-[4-(4-fluorobenzyl)piperazin-1-yl]-3-oxopropenyl]phenyl]acetamide **685534-50-3P**, [5-Chloro-2-[(E)-3-[4-(4-fluorobenzyl)piperazin-1-yl]-3-oxopropenyl]phenyl]urea **685534-51-4P 685534-55-8P**
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685534-61-6P 685534-62-7P 685534-68-3P
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685535-42-6P 685535-45-9P 685535-46-0P
685535-48-2P 685535-51-7P 685535-52-8P
685535-53-9P 685535-54-0P 685535-59-5P
685535-61-9P 685535-63-1P 685535-65-3P
685535-67-5P 685535-70-0P 685535-72-2P
685535-74-4P 685535-76-6P 685535-78-8P
685535-80-2P 685535-82-4P 685535-83-5P
685535-84-6P 685535-85-7P, 5-Chloro-2-[(E)-3-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-3-oxopropenyl]-N-(1-methylpiperidin-4-yl)benzamide **685535-86-8P**, N-(1-Benzylpiperidin-4-yl)-5-chloro-2-[(E)-3-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-3-oxopropenyl]benzamide **685535-87-9P**, 4-[[5-Chloro-2-[(E)-3-[4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-3-oxopropenyl]benzoyl]amino]piperidine-1-carboxylic acid ethyl ester **685535-88-0P**
685535-89-1P 685535-91-5P 685535-93-7P
685535-95-9P, N-[5-Chloro-2-[(E)-3-[4-(4-chlorobenzyl)-2-methylpiperazin-1-yl]-3-oxopropenyl]phenyl]acetamide **685535-98-2P**, N-[5-Chloro-2-[(E)-3-[4-(3-fluorobenzyl)-2-methylpiperazin-1-yl]-3-oxopropenyl]phenyl]acetamide **685536-02-1P**, N-[5-Chloro-2-[(E)-3-[4-(2,4-difluorobenzyl)-2-methylpiperazin-1-yl]-3-oxopropenyl]phenyl]acetamide **685536-06-5P**, N-[5-Chloro-2-[(E)-3-[4-(4-cyanobenzyl)-2-methylpiperazin-1-yl]-3-oxopropenyl]phenyl]acetamide **685536-10-1P**, N-[5-Chloro-2-[(E)-3-[(R)-4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-3-oxopropenyl]-4-methoxyphenyl]acetamide
685536-16-7P 685536-19-0P 685536-23-6P
685536-27-0P 685536-31-6P 685536-33-8P
685536-37-2P 685536-41-8P 685536-48-5P
685536-50-9P 685536-54-3P 685536-56-5P
685536-58-7P 685536-62-3P 685536-66-7P
685536-70-3P 685536-79-2P 685539-57-5P
685842-01-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(CCR-1 antagonist; preparation of (benzylpiperazinyl)phenylpropenones as CCR-1 antagonists for treatment of inflammatory and autoimmune diseases)

IT **685534-23-0P 685534-24-1P 685534-40-1P**
685534-41-2P 685534-44-5P 685534-45-6P
685534-48-9P, [5-Chloro-2-[(E)-3-[4-(4-fluorobenzyl)piperazin-1-yl]-3-oxopropenyl]phenyl]carbamic acid tert-butyl ester
685534-49-0P 685534-54-7P 685534-66-1P
685534-67-2P 685534-73-0P 685534-74-1P
685534-80-9P 685534-81-0P 685534-88-7P

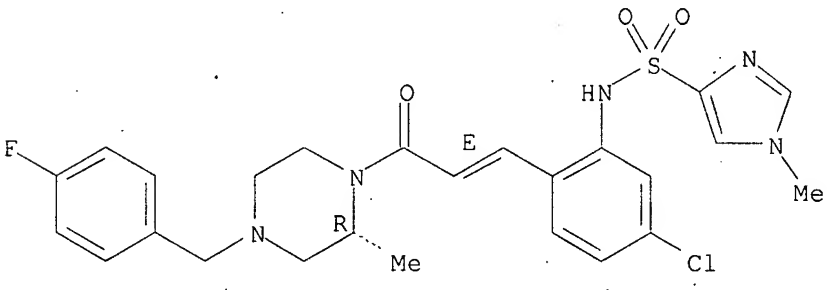
685534-89-8P 685534-91-2P 685534-93-4P
685535-26-6P 685535-31-3P 685535-34-6P
685535-35-7P 685535-36-8P 685535-49-3P
685535-50-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of (benzylpiperazinyl)phenylpropenones as CCR-1 antagonists for treatment of inflammatory and autoimmune diseases)

IT **685534-27-4 685534-37-6 685534-60-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of (benzylpiperazinyl)phenylpropenones as CCR-1 antagonists for treatment of inflammatory and autoimmune diseases)

IT **685534-33-2P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(CCR-1 antagonist; preparation of (benzylpiperazinyl)phenylpropenones as CCR-1 antagonists for treatment of inflammatory and autoimmune diseases)

RN 685534-33-2 HCAPLUS
CN Piperazine, 1-[(2E)-3-[4-chloro-2-[[(1-methyl-1H-imidazol-4-yl)sulfonyl]amino]phenyl]-1-oxo-2-propenyl]-4-[(4-fluorophenyl)methyl]-2-methyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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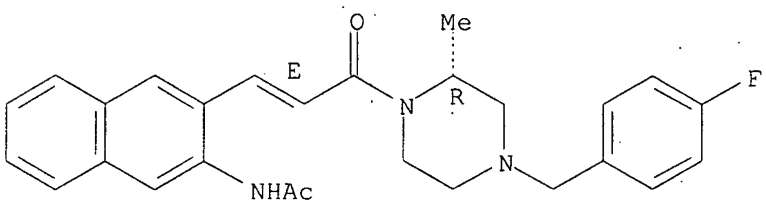
L37 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1144476 HCAPLUS
DN 144:51547
TI Novel CCR1 antagonists with oral activity in the mouse collagen induced arthritis
AU **Revesz, Laszlo; Bollbuck, Birgit**; Buhl, Thomas; **Eder, Joerg**; Esser, Ronald; Feifel, Roland; **Heng, Richard**; Hiestand, Peter; Jachez-Demange, Benedicte; Loetscher, Pius; Sparrer, Helmut; **Schlapbach, Achim; Waelchli, Rudolf**
CS **Novartis Institutes for BioMedical Research, Global Discovery Chemistry, Autoimmunity and Transplantation, Basel, CH-4002, Switz.**
SO Bioorganic & Medicinal Chemistry Letters (2005), 15(23), 5160-5164
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier B.V.
DT Journal
LA English
OS CASREACT 144:51547

AB Cinnamides as novel CCR1 antagonist chemotypes are described with high affinity to human and rodent receptors. Two compds., (2R)-1-[3-[2-[(aminocarbonyl)amino]-4-chlorophenyl]-1-oxo-2-propenyl]-4-[(4-fluorophenyl)methyl]-2-(methyl)piperazine and N-[5-chloro-2-[3-[3-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]octyl]-3-oxo-1-propenyl]phenyl]-2-(dimethylamino)acetamide, showed oral activity in the mouse collagen induced arthritis.

IT **685534-62-7P 685534-76-3P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of [(fluorophenyl)methyl]piperazine derivs. and study of their activity as orally active CCR1 antagonists in collagen-induced arthritis)

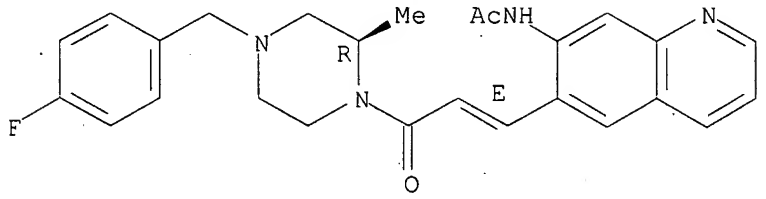
RN 685534-62-7 HCAPLUS
CN Acetamide, N-[3-[(1E)-3-[(2R)-4-[(4-fluorophenyl)methyl]-2-methyl-1-piperazinyl]-3-oxo-1-propenyl]-2-naphthalenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 685534-76-3 HCAPLUS
CN Acetamide, N-[6-[(1E)-3-[(2R)-4-[(4-fluorophenyl)methyl]-2-methyl-1-piperazinyl]-3-oxo-1-propenyl]-7-quinolinyl]- (9CI) (CA INDEX NAME)

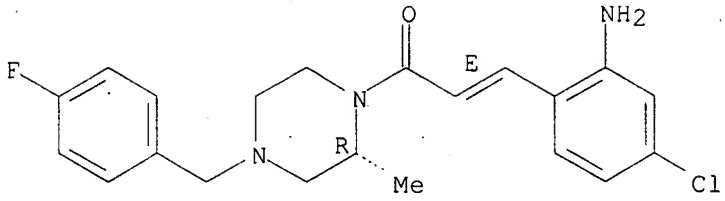
Absolute stereochemistry.
Double bond geometry as shown.



IT **685534-24-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of [(fluorophenyl)methyl]piperazine derivs. and study of their activity as orally active CCR1 antagonists in collagen-induced arthritis model)

RN 685534-24-1 HCAPLUS
CN Piperazine, 1-[(2E)-3-(2-amino-4-chlorophenyl)-1-oxo-2-propenyl]-4-[(4-fluorophenyl)methyl]-2-methyl-, (2R)- (9CI) (CA INDEX NAME)

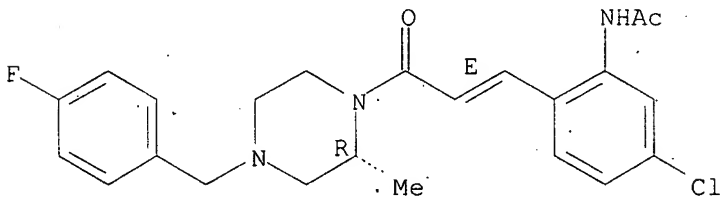
Absolute stereochemistry.
Double bond geometry as shown.



IT **685534-25-2P 685534-42-3P 685534-43-4P**
685534-47-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of [[[chloro(acetylamino)phenoxy]methyl]carbonyl](fluorobenzyl) piperazine derivs. and study of their activity as orally active CCR1 antagonists in collagen-induced arthritis)

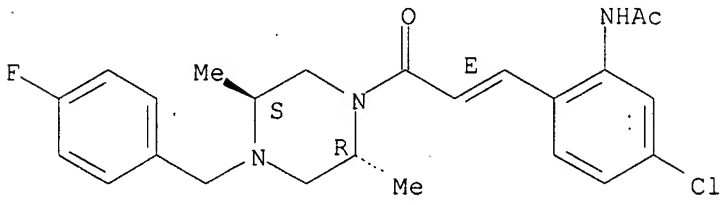
RN 685534-25-2 HCAPLUS
CN Acetamide, N-[5-chloro-2-[(1E)-3-[(2R)-4-[(4-fluorophenyl)methyl]-2-methyl-1-piperazinyl]-3-oxo-1-propenyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



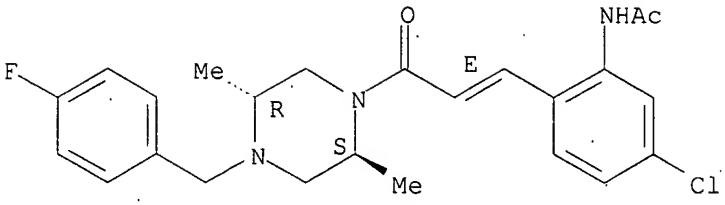
RN 685534-42-3 HCAPLUS
CN Acetamide, N-[5-chloro-2-[(1E)-3-[(2R,5S)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-3-oxo-1-propenyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



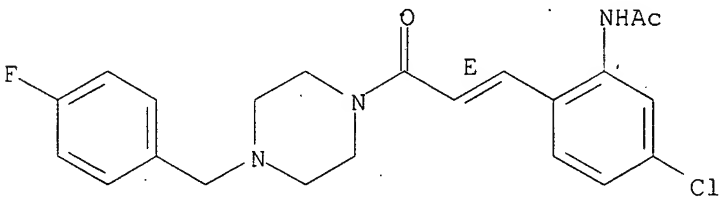
RN 685534-43-4 HCAPLUS
CN Acetamide, N-[5-chloro-2-[(1E)-3-[(2S,5R)-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-1-piperazinyl]-3-oxo-1-propenyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



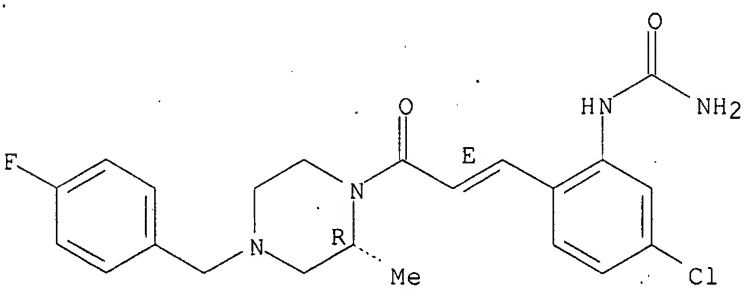
RN 685534-47-8 HCAPLUS
CN Acetamide, N-[5-chloro-2-[(1E)-3-[4-[(4-fluorophenyl)methyl]-1-piperazinyl]-3-oxo-1-propenyl]phenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



IT **685534-28-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of [chloro[(fluorobenzyl)(methyl)piperazinyl]oxopropenyl]phenyl]urea derivative and study of its activity as orally active CCR1 antagonist in collagen-induced arthritis)
RN 685534-28-5 HCAPLUS
CN Piperazine, 1-[(2E)-3-[2-[(aminocarbonyl)amino]-4-chlorophenyl]-1-oxo-2-propenyl]-4-[(4-fluorophenyl)methyl]-2-methyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RETABLE

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Blumberg, L	2002			WO 2002032901	HCAPLUS
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L37 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:962024 HCAPLUS
DN 143:248412
TI Preparation of piperazine derivatives as CCR1 antagonists for the treatment of endometriosis
IN Kaufmann, Ulrike
PA Schering Aktiengesellschaft, Germany; Horuk, Richard
SO PCT Int. Appl., 291 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005079769	A2	20050901	WO 2005-EP2036	20050223
	WO 2005079769	A3	20070104		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, SM				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2005215156	A1	20050901	AU 2005-215156	20050223
	CA 2556423	A1	20050901	CA 2005-2556423	20050223
	EP 1727526	A2	20061206	EP 2005-715567	20050223
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	BR 2005007985	A	20070508	BR 2005-7985	20050223
	JP 2007523126	T	20070816	JP 2006-553572	20050223
	MX 2006PA09687	A	20061030	MX 2006-PA9687	20060824
	IN 2006DN04855	A	20070817	IN 2006-DN4855	20060824

	NO 2006004298	A	20061124	NO 2006-4298	20060922
	KR 2007033961	A	20070327	KR 2006-719708	20060922
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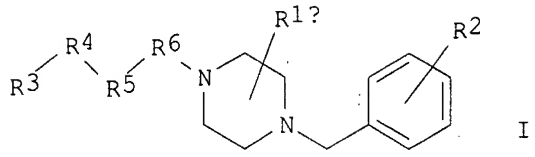
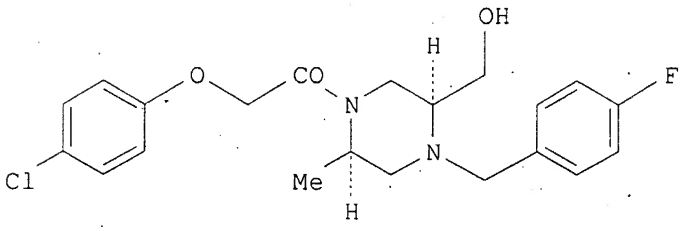
OS MARPAT 143:248412

GI



I



II

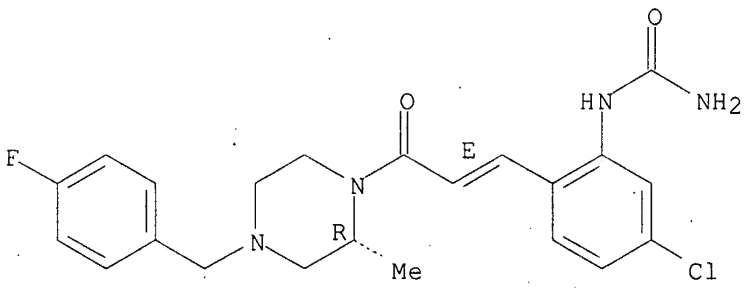
AB The use is claimed of piperazine derivs. (shown as I; variables defined below; e.g. (2R,5S)-1-[[(4-chlorophenoxy)methyl]carbonyl]-2-methyl-4-(4-fluorobenzyl)-5-[(hydroxy)methyl]piperazine (shown as II)) for the production of a medicament for the treatment of endometriosis in humans wherein the treatment comprises administering to a human female in need of such treatment a therapeutically effective amount of said compound Compds. I inhibit the activity of the chemokines MIP-1α and RANTES and thus are antagonists of human chemokine "C-C" receptor 1 (CCR1): For I: R1a is ≥1 substituents = oxo, halo, (C1-C8)alkyl, (C3-C10)cycloalkyl, (C3-C10)cycloalkyl(C1-C8) alkyl, (C3-C10)cycloalkylamino(C1-C8)alkyl, [(C3-C10)cycloalkyl(C1-C8) alkyl]amino(C1-C8)alkyl, halo(C1-C8)alkyl, (C2-C8)alkenyl, (C2-C8)alkynyl, et al.; R2 is ≥1 substituents = H, hydroxy, hydroxysulfonyl, halo, (C1-C8)alkyl, mercapto, mercapto(C1-C8)alkyl, (C1-C8)alkylthio, (C1-C8)alkylsulfinyl, (C1-C8)alkylsulfonyl, (C1-C8)alkylthio(C1-C8)alkyl, (C1-C8)alkylsulfinyl(C1-C8)alkyl, (C1-C8) alkylsulfonyl(C1-C8)alkyl, et al.; R3 is a carbocyclic 3- to 15-membered ring system substituted by ≥1 H, hydroxy, hydroxysulfonyl, halo, (C1-C8)alkyl, mercapto, mercapto(C1-C8)alkyl, (C1-C8)alkylthio, et al.; R4 is -O-, -N(R7)-, -C(R8)2- or a bond; R5 is an (C1-C8) alkylene chain or an (C1-C8) alkylidene chain, or, if R4 is a bond, R5 is an (C1-C8) alkylidene chain (un)substituted by (un)substituted Ph or naphthyl or -N(R7)2; or R4 and R5 together are -HC:CH-; R6 is -C(O)-, -C(S)-, -CH2- or a bond; addnl. details are given in the claims. Although the methods of preparation are not claimed, 16 example prepns. and characterization data for a large number of I are included. For example, II was prepared (79 % yield) by N-acylation of (2R,5S)-1-(4-fluorobenzyl)-2-[(hydroxy)methyl]-5-methylpiperazine by 4-chlorophenoxyacetyl chloride.

IT **685534-28-5P**, [5-Chloro-2-[(E)-3-[(R)-4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-3-oxoprop-1-enyl]phenyl]urea **685534-31-0P**, N-[5-Chloro-2-[(E)-3-[(R)-4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-3-oxoprop-1-enyl]phenyl]methanesulfonamide **685534-39-8P**, [5-Chloro-2-[(E)-3-[(2R,5S)-4-(4-fluorobenzyl)-2,5-dimethylpiperazin-1-yl]-3-oxoprop-1-enyl]phenyl]urea **685534-96-7P**, N-[5-Chloro-2-[(E)-3-

[(2R,5S)-4-(4-fluorobenzyl)-2,5-dimethylpiperazin-1-yl]-3-oxoprop-1-enyl]phenyl]methanesulfonamide **685535-82-4P**, 5-Chloro-2-[(E)-3-[(R)-4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-3-oxoprop-1-enyl]benzoic acid **685536-19-0P**, [5-Chloro-2-[(E)-3-[(R)-4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-3-oxoprop-1-enyl]-4-methoxyphenyl]urea **685536-37-2P**, [5-Chloro-2-[(E)-3-[(R)-4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-3-oxoprop-1-enyl]-4-trifluoromethoxyphenyl]urea **685536-74-7P**, 5-Chloro-2-[(E)-3-[(R)-4-(4-fluorobenzyl)-2-methylpiperazin-1-yl]-3-oxoprop-1-enyl]-4-methoxybenzoic acid methyl ester
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of piperazine derivs. as CCR1 antagonists for treatment of endometriosis)

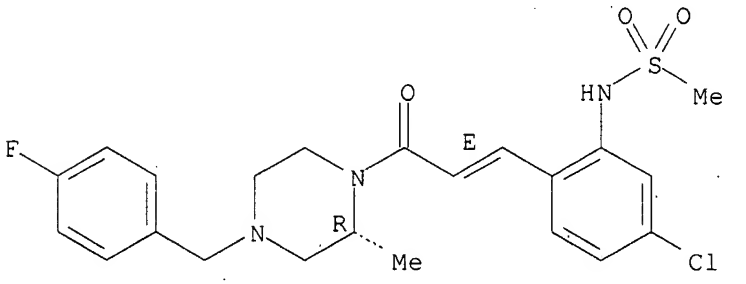
RN 685534-28-5 HCAPLUS
CN Piperazine, 1-[(2E)-3-[2-[(aminocarbonyl)amino]-4-chlorophenyl]-1-oxo-2-propenyl]-4-[(4-fluorophenyl)methyl]-2-methyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



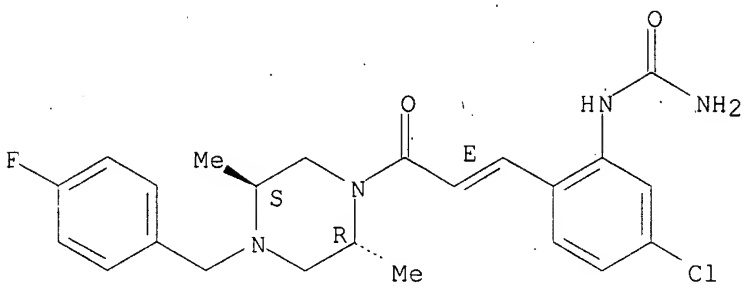
RN 685534-31-0 HCAPLUS
CN Piperazine, 1-[(2E)-3-[4-chloro-2-[(methylsulfonyl)amino]phenyl]-1-oxo-2-propenyl]-4-[(4-fluorophenyl)methyl]-2-methyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



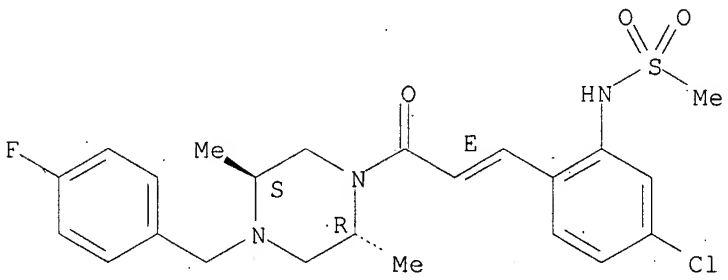
RN 685534-39-8 HCAPLUS
CN Piperazine, 1-[(2E)-3-[2-[(aminocarbonyl)amino]-4-chlorophenyl]-1-oxo-2-propenyl]-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-, (2R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



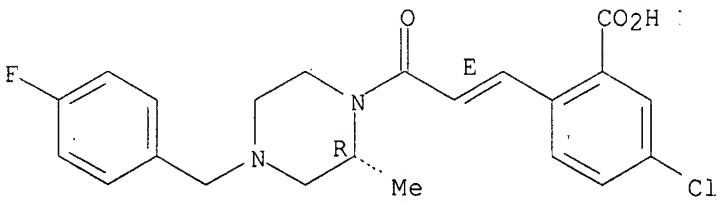
RN 685534-96-7 HCAPLUS
CN Piperazine, 1-[(2E)-3-[4-chloro-2-[(methylsulfonyl)amino]phenyl]-1-oxo-2-propenyl]-4-[(4-fluorophenyl)methyl]-2,5-dimethyl-, (2R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



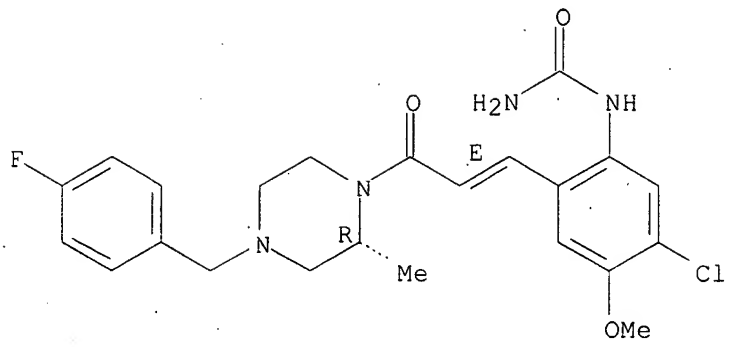
RN 685535-82-4 HCAPLUS
CN Benzoic acid, 5-chloro-2-[(1E)-3-[(2R)-4-[(4-fluorophenyl)methyl]-2-methyl-1-piperazinyl]-3-oxo-1-propenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



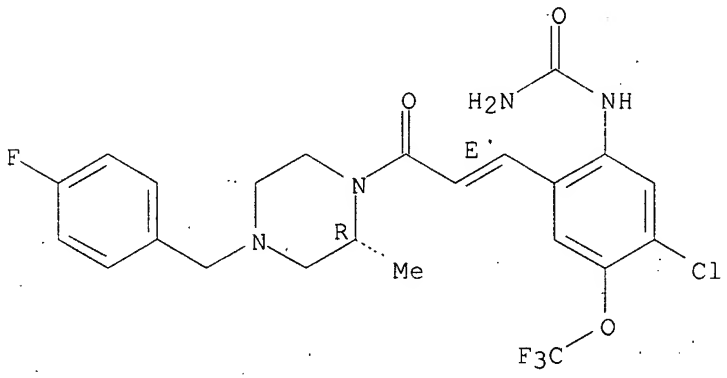
RN 685536-19-0 HCAPLUS
CN Piperazine, 1-[(2E)-3-[2-[(aminocarbonyl)amino]-4-chloro-5-methoxyphenyl]-1-oxo-2-propenyl]-4-[(4-fluorophenyl)methyl]-2-methyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



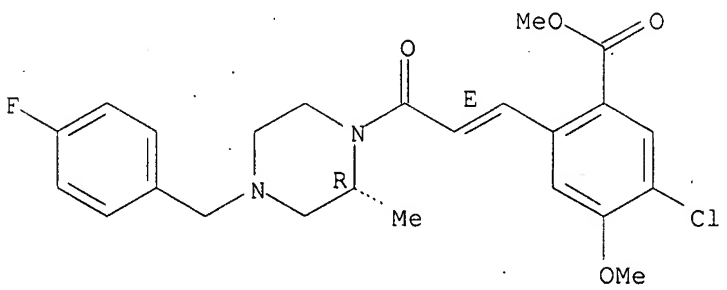
RN 685536-37-2 HCAPLUS
CN Piperazine, 1-[(2E)-3-[2-[(aminocarbonyl)amino]-4-chloro-5-(trifluoromethoxy)phenyl]-1-oxo-2-propenyl]-4-[(4-fluorophenyl)methyl]-2-methyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 685536-74-7 HCAPLUS
CN Benzoic acid, 5-chloro-2-[(1E)-3-[(2R)-4-[(4-fluorophenyl)methyl]-2-methyl-1-piperazinyl]-3-oxo-1-propenyl]-4-methoxy-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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L50 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 1986:33908 HCAPLUS
DN 104:33908
TI Naphthalene derivatives
IN Hashimoto, Kinji; Goto, Kyoto; Tsuda, Yoshiaki
PA Otsuka Pharmaceutical Factory, Inc., Japan
SO Jpn. Kokai Tokkyo Koho, 13 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 60139646	A	19850724	JP 1983-248760	19831227
	JP 03014296	B	19910226		
PRAI	JP 1983-248760		19831227		

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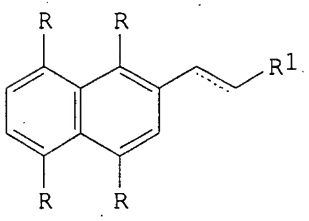

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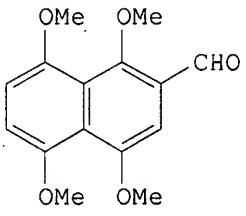
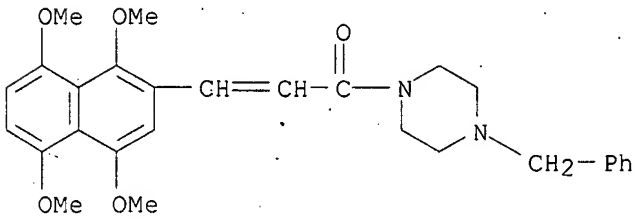


II

AB Naphthalene derivs. (I; R = alkoxy; R1 = CO2H, NO2, carbamoyl, dialkylcarbamoyl, etc.), effective vasodilators, thromboxane A2 biosynthesis inhibitors, cardiotonics, etc. (no data), were prepared Thus, 20 mmol II and 0.3 mL piperidine were added to a solution of 40 mmol malonic acid in pyridine at 80-85° and refluxed 3 h to give 5 g I (R = MeO, R1 = CO2H, unsatd. side chain).

IT **99724-01-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 99724-01-3 HCAPLUS
CN Piperazine, 1-[1-oxo-3-(1,4,5,8-tetramethoxy-2-naphthalenyl)-2-propenyl]-4-(phenylmethyl)- (9CI) (CA INDEX NAME)



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                E E5+ALL
L2         74401 S E26+RT OR E26-E225/PA,CS
                E NOVARTI/CO
L3          6538 S E229 OR NOVARTIS?/PA,CS,CO
                E BOLLBUCK/AU
L4            13 S E241,E242
                E EDER/AU
L5            45 S E3
                E EDER J/AU
L6           198 S E264-E268,E276,E280
                E HENG/AU
                E HENG R/AU
L7            21 S E444,E445
                E REVESZ/AU
                E REVESZ L/AU
L8           157 S E468-E470
                E REVES/AU
                E REVEZ/AU
                E SCHLAPBACH/AU
L9            22 S E505,E506
                E WALCHLI/AU
L10            2 S E533
                E WAELCHLI/AU
L11           26 S E563,E563,E566,E567
L12            1 S L1 AND L2-L11

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L16            50 S L15
L17               STR L15
L18            50 S L17
L19          2323 S L17 FUL
                SAV TEMP L19 SACKEY532A/A
L20           141 S L14 AND L19
L21               STR L17
L22            23 S L21 SAM SUB=L19
L23               STR L21
L24            14 S L23 SAM SUB=L19
L25           334 S L23 FUL SUB=L19
                SAV TEMP L25 SACKEY532B/A
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L30             2 S L29 AND L1-L12
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L31             1 S L29 NOT L30
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L33             0 S L29-L31 AND PY<=2002 NOT P/DT
L34             1 S L29-L31 AND (PD<=20031024 OR PRD<=20031024 OR AD<=20031024) A
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L36             1 S L34,L35
L37             2 S L29-L31 NOT L36

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L39            28 S L26
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L45            11 S L39 AND (PD<=20021025 OR PRD<=20021025 OR AD<=20021025) AND P
L46            16 S L43-L45
L47             0 S L40 AND L46
                  SEL HIT RN L46

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L48            21 S E574-E594
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L57            17 S L56 AND L26

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